Kongeriget Danmark

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Applicant: (Name and address)
Coloplast A/S
Holtedam 1
DK-3050 Humlebæk
Denmark

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30 December 2003

Pia Høybye-Olsen

PATENT- OG VAREMÆRKESTYRELSEN

TITLE

A catheter with a pharmaceutically active composition.

BACKGROUND OF THE INVENTION

1. Field of the Invention

Women with neurogenic bladder dysfunction, e.g. because of Spinal Cord Injury or Multiple Sclerosis use intermittent catheterisation as first choice of method when emptying the bladder.

Unfortunately, many of these women have episodes of incontinence in between catheterisations. These problems are more pronounced for women than for men with the same diseases. And the problem is rising with increasing age.

At the time being there is no good female alternative to the male collecting device (uri-sheaths / urinary condoms). The only solution is to wear pads or diapers, which has a negative impact on quality of life.

The uro-genital oestrogen deficiency syndrome includes local urogenital symptoms, appearing in 25-50% of all menopausal women. The symptoms are caused by the lack of oestrogen and they result in atrophy of the epithelium in both vagina and urethra. The symptoms include dryness, discomfort, pain, recurrent urinary tract infections, urge incontinence and stress incontinence (frequent urinations and urinations during night time).

The problem could be overseen in this group of patients, because of their primary bladder dysfunction, impaired sensation and basic incontinence. The risk of urinary tract infections is also increased because of catheterisations, large residual urine volumes and high intravesical pressures.

It is recommended for healthy women to perform bladder and pelvic floor exercises. This is, however, not possible for Spinal Cord Injured women, so this effect is unachievable. Especially for women with low lesions, the bladder and pelvic musculature is paralysed with no reflex activity and therefore no muscle tone.

In summary, the oestrogen deficiency symptoms in the urogenital area, including urge- and stress incontinence, increased risk of infections and mucosal dryness and pain, are difficult to recognize in women with neurogenic bladder dysfunction. Treating these symptoms could be beneficial for especially the older women with SCI or MS, in reducing incontinence episodes.

The proliferative mucosal effect of oestrogen supplementation might also have a positive influence on fertile women with neurogenic dysfunction, but this is an area, yet to be explored.

2. Description of the Related Art

The Urogenital Oestrogen Deficiency Syndrome in itself is often solved by treating with systemic or vaginal administration of oestrogen or oestrogen-derivatives, such as Oestriol or Oestradiol.

It is known that Oestriol or Oestradiol treatment increases the mobility of the urethro-vesical junction[1] increases the thickness of urethral mucosa[2], increases urethral vascularisation[1], alleviates subjective and objective symptoms[2], restores vaginal pH[2] and decreases leakage episodes[5] and urinary incontinence complaints[5].

The results are, however, varying depending on the administration route, but it can be concluded that vaginal administration bypasses the first liver metabolism and is therefore more potent and shows better results and lesser side effects[6].

Other pharmaceutically active agents used for treatment of the continence system by a group of male and female users of intermittent catheterisation include anticholinergical drugs and capsaicin.

[1] Martan A, Masata J, Halaska M, Voigt R. Ultrasound imaging of the lower urinary tract in post-menopausal women with urinary stress or combined type of incontinence before and after intravaginal administration of estrio. Ceska Gynekol.1999 Jan;64(1):6-9.,[1]

[2] Henriksson L., Stjernquist M. Boquist L, Alander U, Silenus I. A comparative multicenter study of the effects of continous low-dose estradiol released from a

new vaginal ring versus estriol vaginal pessaries in postmenopausal women with symptoms and signs of urogenital atrophy. Am J Obstet Gynecol.1994 Sep;171(3):624-32.

3. van der Linden MC, Gerretsen G, Brandhorst MS, Ooms EC, Kremer CM, Doesburg WH. The effect of estriol on the cytology of urethra and vagina in postmenopausal women with genito-urinary symptoms. Eur J Obstet Gynecol Reprod Biol. 1993 Sep;51(1):29-33.

4. Heimer GM, Englund DE. Effects of vaginally-administered oestriol on postmenopausal urogenital disorders: a cytohormonal study. Maturitas 1992 Mar;14(3):171-9.

[5] Ahlstom K, Sandahl B, Sjoberg B, Ulmsten U, Stormby N, Lindskog M. Effect of combined treatment with phenylpropanolamine and estriol, compared with estriol treatment alone, in postmenopausal women with stress urinary incontinence. Gynecol Obstet Invest. 1990;30(1):37-43.

[6] Heimer GM. Estriol in the menopause. Acta Obstet Gynecol Scand Suppl 1987;139:1-23.

SUMMARY OF THE INVENTION

By coating an intermittent catheter with Oestriol, the active ingredient is delivered to the urethral mucosa directly and this treatment could alleviate the symptoms caused by urethral atrophy in between the catheterisations.

The primary effect of the device is drainage of urine, the secondary effect is supplying the urethral epithelium with oestriol to achieve better continence in between catheterisations by mucosal proliferation and additional effects as described above.

Compared to known treatments, the purpose of urethral administration is to achieve better effect on urological symptoms than vaginal or oral administration, and to avoid the side effects seen by systemic administration.

Brief Description of the Drawings

The invention is disclosed more in detail with reference to the drawings in which Fig 1-4 shows examples of patterns formed by zones of active ingredients (1) on a tubular catheter element (12) with eyes (9).

Fig 5 shows a package with a compartment (5) containing a gel. The compartment has a tip (2), which is removed before use and a sealing (3) which is broken as the catheter element (4) is pushed through the compartment containing the gel (1).

Fig 6 shows a cross section (length direction) of a catheter element (6) without eyes and with a pill (7) placed on the proximal end of the catheter element and a film (8) covering the pill.

Fig 7 shows a cross section (perpendicular to the length direction) of a wing catheter (10) with a substance containing active ingredients in the concave corner (11).

Detailed Description of the Present Invention

This invention relates to a device for urinary catheterisation, comprising a pharmaceutically active composition and a catheter element adapted to be inserted in the urethra and to deliver the pharmaceutically active composition in the lower urinary tract system during catheterisation.

The type of catheter element is not essential to the invention and could be of any type, such as disclosed in PCT/DK02/00449. In addition to tubular catheters for which the drainage canal is defined by the catheter material, preferable embodiments of the present invention could comprise a catheter element of wing catheter type, for which the urethra form a part of the drainage canals.

In one embodiment of the invention, the catheter device should be able to deliver the active substance very quickly, i.e. in less than 2 minutes, which is the average normal time for intermittent catheterisation. The active ingredient should preferably work in the urethra for approx. 2-4 hours, in between catheterisations. In another embodiment of the invention the active substance is released more slowly and the time spend by the catheter element in the urethra by intermittent

catheterisation is extended. In a further embodiment the release of the active agents is adapted to take place with the catheter element permanently placed in the urethra.

The present invention allows for medical treatment of the continence system. In a first embodiment of the invention, the active composition contains active agents for treatment of the urethral mucosa, such as agents effective against urethral atrophy. Certain hormones have proven valuable for preventing and treating urethral atrophy. Examples include oestrogens and oestrogen derivatives such as oestriol or oestradiol.

In a second embodiment at least a part of the active composition of the present invention could be selected to have an effect on the unstriated musculature or the neuromuscular junction. Examples of sucg active ingredients with a desired effect comprise anticholinergical drugs and capsaicin.

In one embodiment of the invention, at least a part of the active composition is provided in a coating covering at least a portion of the surface of the catheter element. This coating could be a polymer coating, of which at least a portion is impregnated with at least a part of the active composition. At least a portion of the catheter could have a hydrophilic coating adapted to reduce friction between the catheter element and urethra for a more comfortable insertion. In one embodiment of the present invention this hydrophilic coating or the swelling medium for swelling the hydrophilic coating contain active ingredients. In another embodiment of the present invention a hydrophilic coating and a coating containing the active ingredients could be applied to the catheter element in an alternating pattern to create zones adapted to deliver active ingredients alternating with zones adapted to reduce friction. Examples of patterns of distribution are shown in Fig 1-4. The zones of active ingredients could be constrained to a part of the catheter element such as the tip. The coating containing active ingredients could have hydrophobic properties, e.g. for resistance to a liquid swelling medium.

In another embodiment at least a part of the active composition is provided in a gel or crème adapted for application to at least a portion of the catheter element. In a preferred embodiment the active composition is integrated in a gel that prelubricates the catheter element to reduce friction between the catheter element and urethra for a more comfortable insertion. The catheter doesn't need a hydrophilic coating, since the gel in itself would provide the lubricating effect. In one embodiment of the present invention the gel is applied in the production procedure. In another embodiment the gel and the catheter element is provided in a catheter assemblage adapted for application of the gel to the catheter element prior to use by the person performing the catheterisation. An example is a catheter package including an Oestriol-containing gel. In an embodiment of the invention the gel is provided in a separate container adapted for application of the gel to the catheter element by squeezing the container. In another embodiment the package hosting the catheter element has a compartment adapted to hold the gel. In a further embodiment the gel is applied to the catheter element by pressing the catheter element through the compartment containing the gel. An example of this solution is shown in Fig 5.

In another embodiment the catheter element has depressions on the outer surface, which are adapted to hold at least a part of the active agents. In case of a wing catheter active ingredients could be provided in the concave corners of the catheter as shown in Fig 7. Fig 1-4 gives examples of a tubular catheter with depressions forming a pattern of zones containing at least one active ingredient. In a further embodiment of the invention, release of the active ingredients in the urethra is promoted by an consistency regulating agent, which e.g. become more viscous when warmed to body temperature, and is either used in the matrix or as a slip layer between catheter element and the pharmaceutical composition or as a cover on top of the active ingredients which is melted or dissolved by contact with urine and/or body heat.

In another embodiment of the invention, at least a part of the pharmaceutically active composition is provided in a separate unit, such as a pill or ampoule, and the catheter device is adapted to insert this unit in the lower urinary tract system. In one embodiment a pill could be placed on the tip of the catheter and capped with a film, which is dissolved or melted by contact with urine and/or body heat, such as PVA. An example of this embodiment is shown in Fig 6. This solution has the advantage that a tubular catheter element does not need eyes, i.e. drainage holes in the side of the tubular member, since the pill provide a rounded end of the catheter element for comfortable insertion. Hence the catheter can be made about 2 cm shorter and discomfort due to the eyes is avoided.

Claims

1. A device for urinary catheterisation, said device comprising a catheter element adapted to be inserted in the urethra, characterised in that said device is comprising a pharmaceutically active composition and said catheter element is adapted to deliver said active composition in the lower urinary tract system during catheterisation.
2. A device according to claim 1, wherein at least a part of said pharmaceutically active composition has an effect on the continence system.
3. A device according to claim 1 or 2, wherein at least a part of said pharmaceutically active composition is effective against urethral atrophy.
4. A device according to any of the preceding claims, wherein at least a part of said pharmaceutically active composition is a hormone.
5. A device according to any of the preceding claims, wherein at least a part of said pharmaceutically active composition is oestrogen or an oestrogen derivative such as oestriol or oestradiol.
6. A device according to any of the preceding claims, wherein at least a part of said pharmaceutically active composition has an effect on the unstriated musculature.

7. A device according to any of the preceding claims, wherein at least a part of said pharmaceutically active composition has an effect on the neuromuscular junction.
8. A device according to any of the preceding claims wherein at least a part of said pharmaceutically active composition is selected among anticholinergical drugs and capsaicin.
9. A device according to any of the preceding claims, wherein said catheter element has a coating covering at least a portion of the surface and said coating contains at least a part of said pharmaceutically active composition and is adapted to release said pharmaceutically active composition within the lower urinary tract system.
10. A device according to any of the preceding claims, wherein at least a part of said catheter element has a polymer coating, and at least a portion of said polymer coating is impregnated with at least a part of said pharmaceutically active composition.
11. A device according to any of the preceding claims, wherein said device is comprising a hydrophilic coating of at least a portion of said catheter element.
12. A device according to claim 11, wherein said hydrophilic coating is impregnated with at least a part of said pharmaceutically active composition.
13. A device according to any of the preceding claims, wherein said catheter element has depressions on the outer surface, which are adapted to hold at least a part of said pharmaceutically active composition.
14. A device according to any of the preceding claims, wherein at least a part of said pharmaceutically active composition is provided in a gel or crème adapted for application to at least a portion of the catheter element.
15. A device according to any of the preceding claims, wherein said device is comprising a lubricating gel adapted to reduce friction between the catheter element and urethra, and said gel is containing at least a part of said pharmaceutically active composition.

16. A device according to any of the preceding claims, wherein said device is comprising a unit containing said pharmaceutically active composition said device is adapted to shed said unit in the lower urinary tract system.

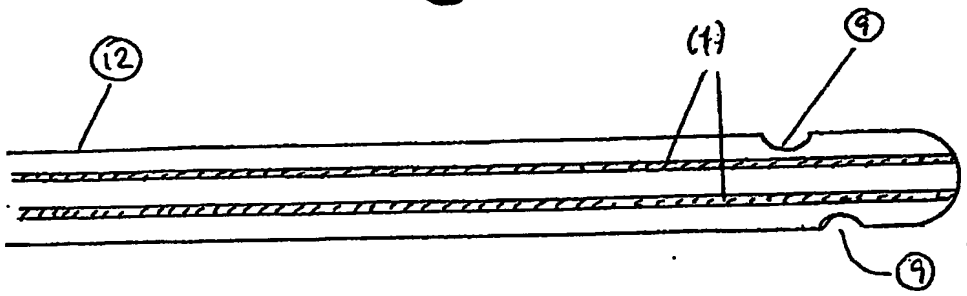

Fig 1

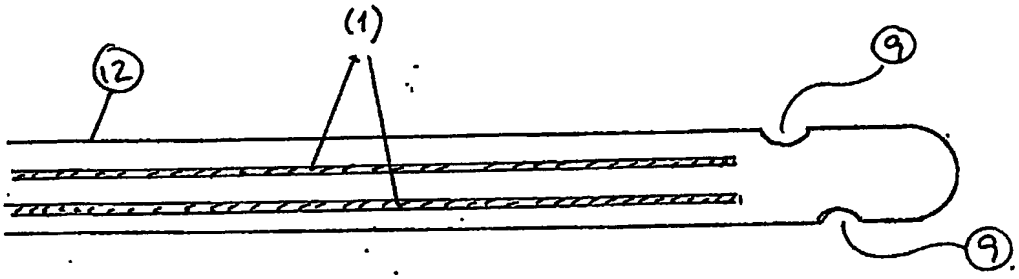

Fig 2

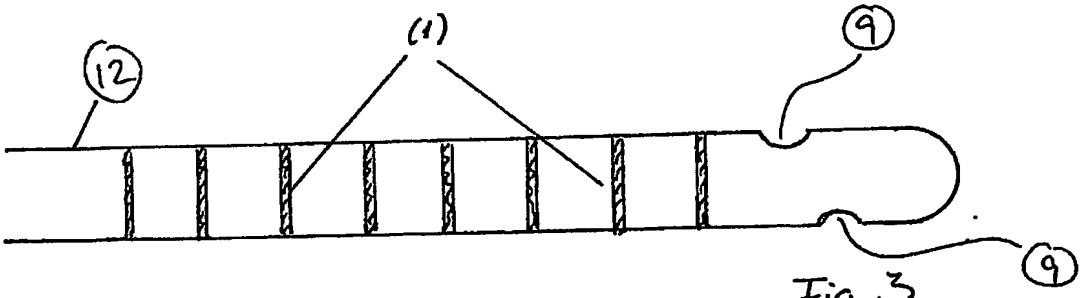

Fig 3

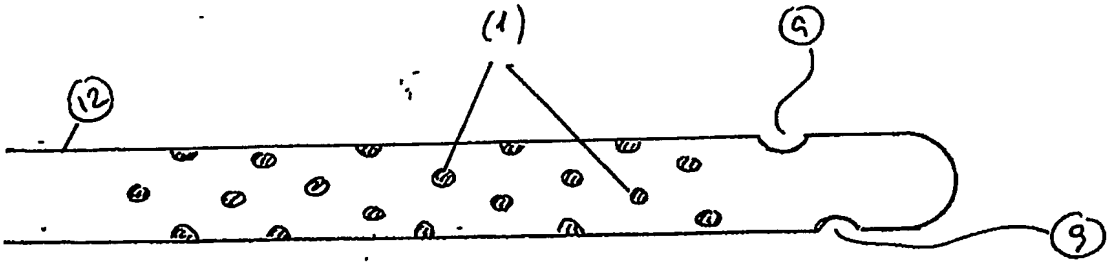

Fig 4

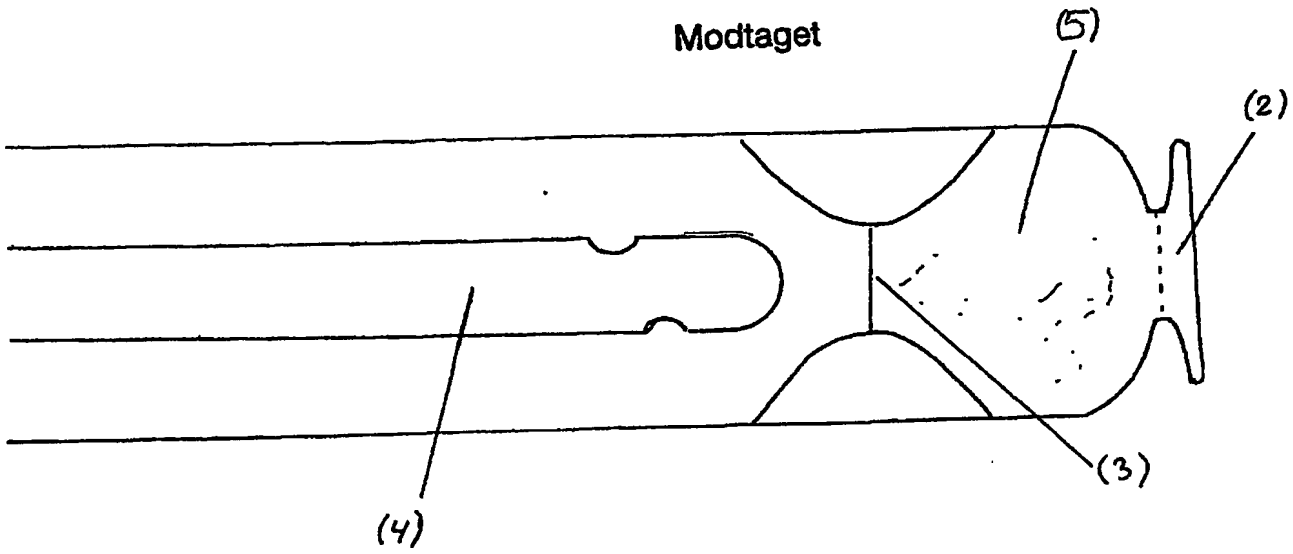

Fig 5

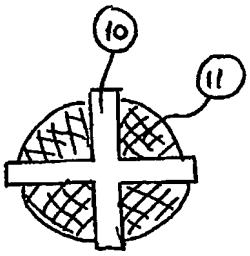

Fig 7

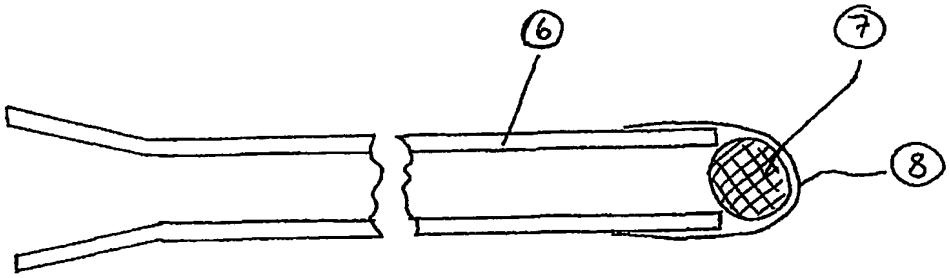

Fig 6